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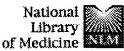
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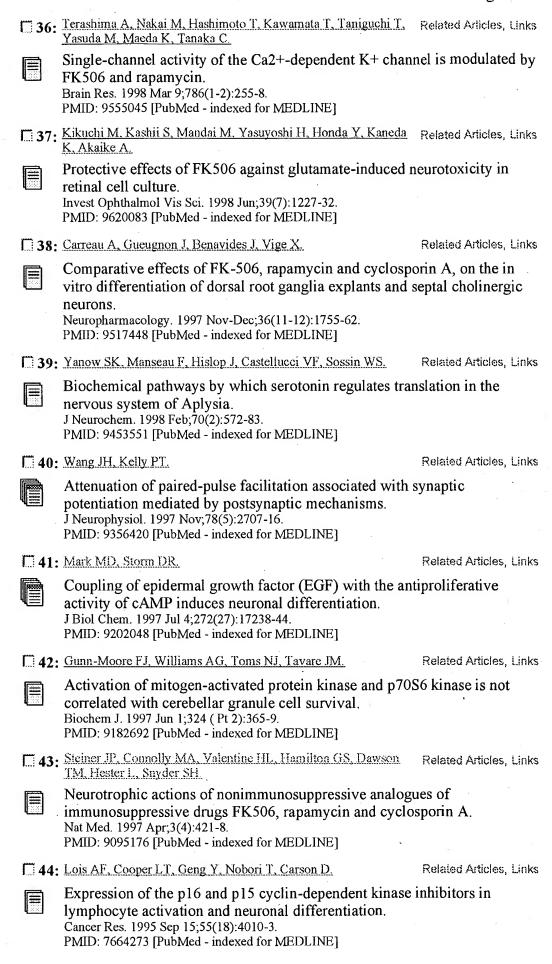
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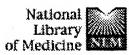
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Neurotrophic actions of nonimmunosuppressive analogues of immunosuppressive drugs FK506, rapamycin and cyclosporin A.

Steiner JP, Connolly MA, Valentine HL, Hamilton GS, Dawson TM, Hester L, Snyder SH.

Department of Neurobiological Research, Guilford Pharmaceuticals Inc., Baltimore, Maryland 21224, USA.

We show that the nonimmunosuppressive analogues of the immunosuppressive drugs FK506, rapamycin and cyclosporin A promote neurite outgrowth both in PC12 cells and sensory neuronal cultures of dorsal root ganglia with potencies resembling their immunosuppressive homologues. Neurotrophic potencies of the immunophilin ligands resemble their potencies in binding to and inhibiting the rotamase activity of FKBP-12 of cyclophilin. Since nonimmunosuppressive immunophilin ligands, which are devoid of calcineurin inhibitory activity, are equally neurotrophic, inhibition of calcineurin activity is not the mediator of the neurotrophic effects. The immunophilin ligands are neurotrophic in intact animals. FK506 and L-685,818 (the C18-hydroxy, C21-ethyl derivative of FK506) treatment of rats with crushed sciatic nerves enhances both functional and morphologic recovery. The striking potency of these agents, their bioavailability and the dissociation of neurotrophic from immunosuppressant actions argue for their therapeutic relevance in the treatment of neurodegenerative diseases.

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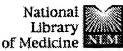
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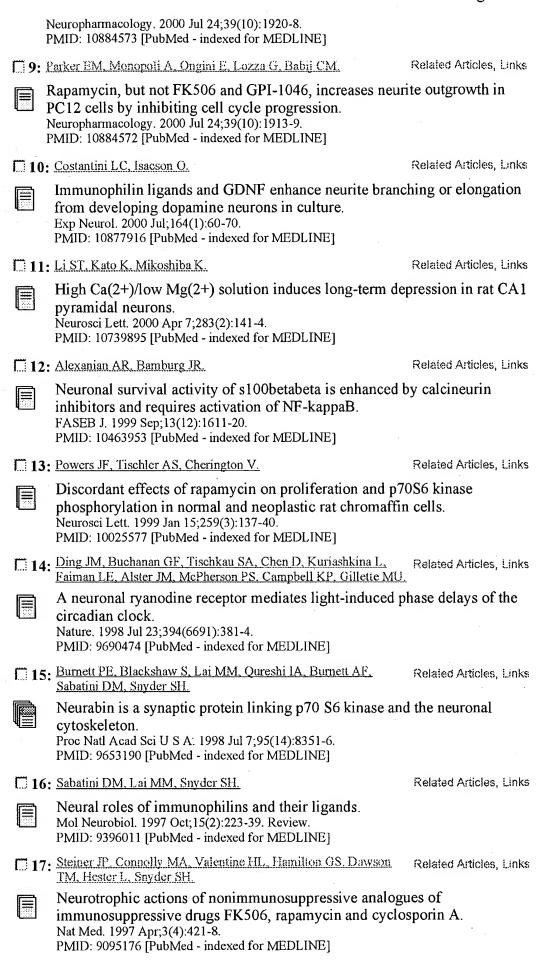
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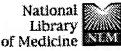
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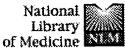
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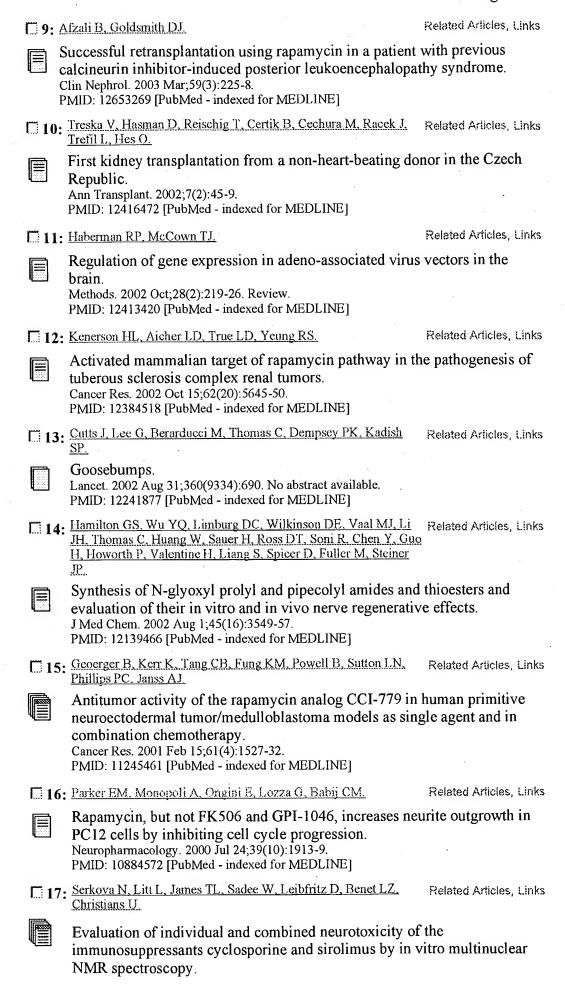
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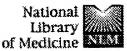
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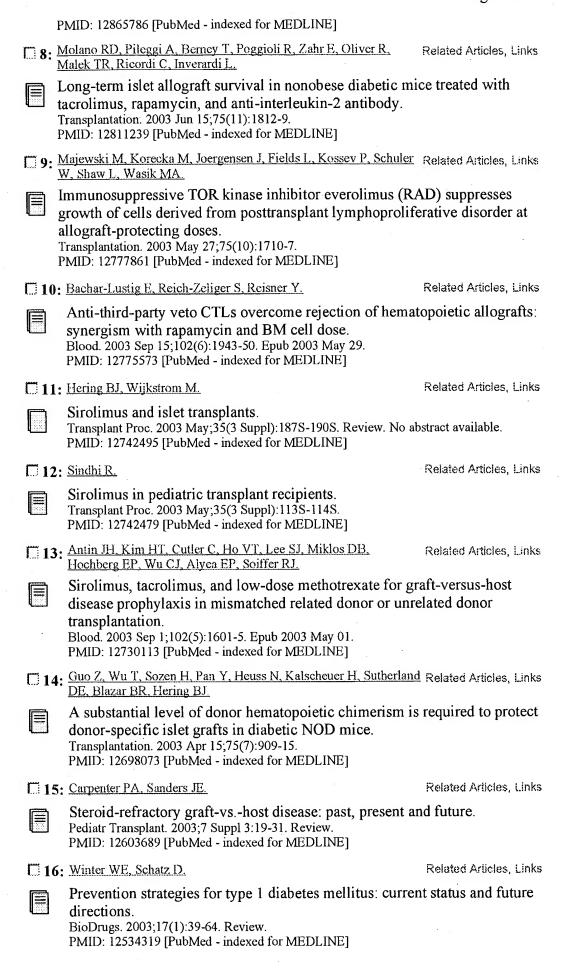
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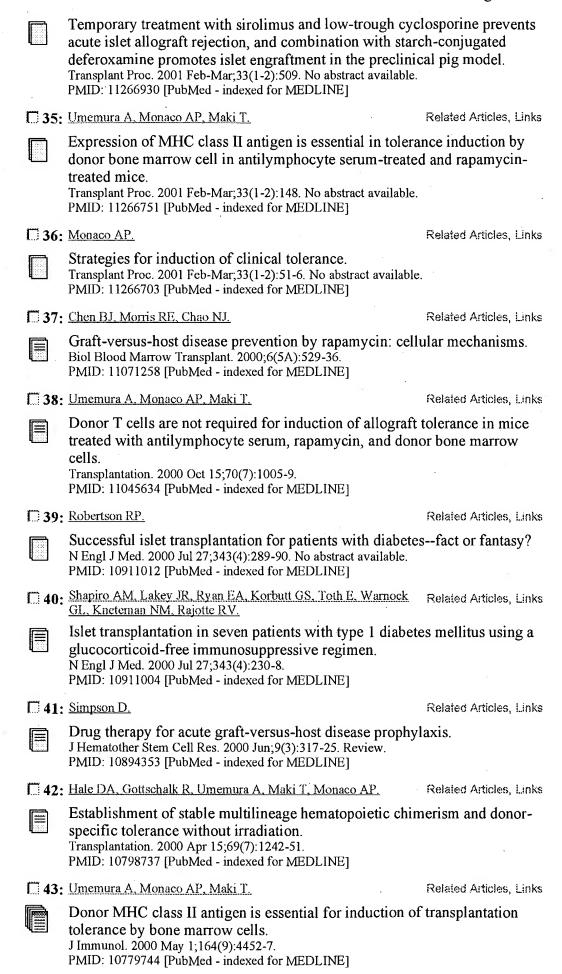
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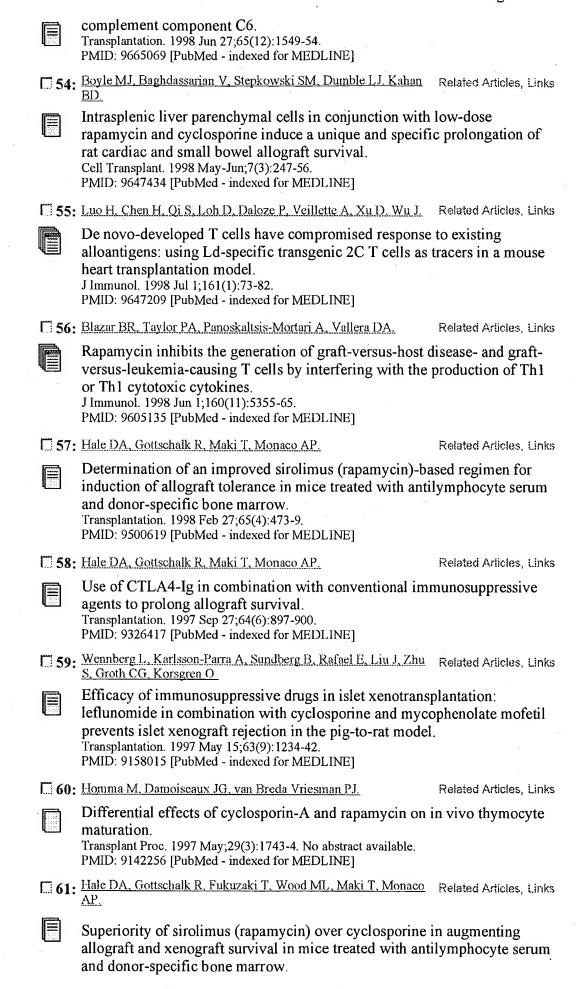
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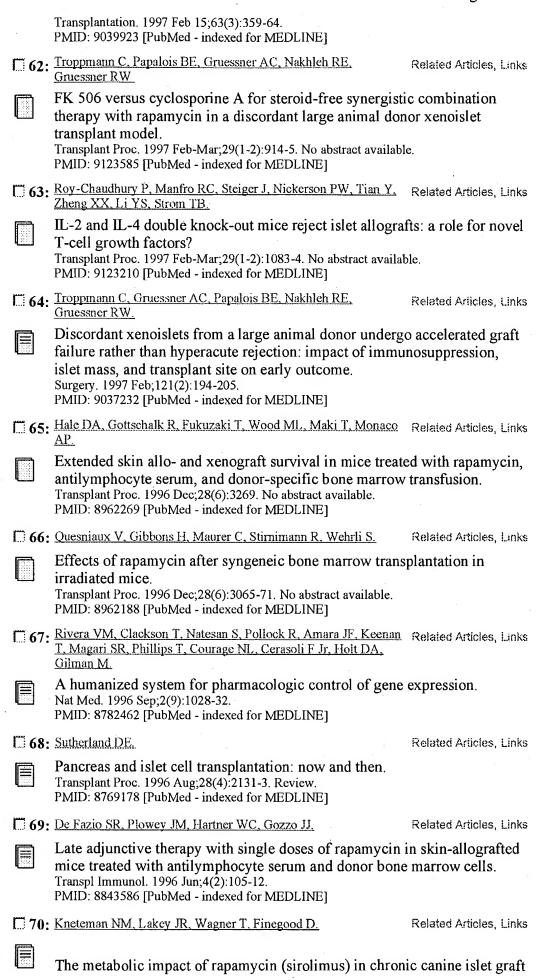


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